



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,937	11/07/2008	Victoria Yamazaki	54795-8003.US00	9737
79975	7590	10/25/2010		
King & Spalding LLP P.O. Box 889 Belmont, CA 94002-0889			EXAMINER KIM, ALEXANDER D	
			ART UNIT	PAPER NUMBER
			1656	
			MAIL DATE	DELIVERY MODE
			10/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/588,937	Applicant(s) YAMAZAKI ET AL.	
	Examiner ALEXANDER D. KIM	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 September 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 7-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 August 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/04/2007, 08/25/2008, 06/12/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a requirement for Restriction/Election (mailed on 04/07/2010), Applicants filed a response and amendment received on 09/07/2010. In said amendment, claim 1 is amended.

Claims 1-14 are pending in the instant Office action.

Election

2. Applicant's election of Group I (claims 1-6) and species (CHO cells for claim 4; and epidermal growth factor for claim 5) with traverse is acknowledged. Because applicant did not distinctly and specifically point out the status of traverse in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)).

Claims 1-14 are pending in the instant application. Claims 7-14 are withdrawn from consideration as non-elected inventions.

Claims 1-6 will be examined herein.

Priority

3. The instant application is a 371 filing of the International Application No. PCT/US05/04497 filed on 2/9/2005, which claims benefit of 60/543,324 filed on 2/9/2005 as requested in the declaration. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S.

filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Applicant's claim no foreign priority under 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

4. The information disclosure statements (IDSs) filed on 09/04/2007, 08/25/2008 and 06/12/2009 has been reviewed, and its references have been considered except for those which have been lined through. A copy of Form PTO/SB/08 is attached to the instant Office action.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See instant specification page 6, lines 7 and 15, reciting "www.wikipedia.com".

Claim Objections

6. Claims 2-3 are objected to because of the following informalities:

(a) Claim 2 recites the abbreviation "GPI". Abbreviations, unless otherwise obvious and/or commonly used in the art, e.g., "DNA", should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used in its first appearance in the claims.

(b) Claim 3 recites "the 32 terminal amino acids...". According to MPEP §1.809 of Patent Rules, it is noted that " Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application."

(c) Claim 4 recites the abbreviation "CHO". Abbreviations, unless otherwise obvious and/or commonly used in the art, *e.g.*, "DNA", should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used in its first appearance in the claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-6 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 1 (Claims 2-6 dependent therefrom) recites "5' signal sequence", "a purification epitope tag ...a 3' anchor sequence". An expression vector consists

of nucleic acid sequence encodes a polypeptide having a function of signal, purification epitope tag and/or anchor sequence. It is wholly unclear how a nucleotide sequence itself can be signal, purification epitope tag and/or anchor sequence. Are they supposed to be ---a 5' nucleic acid sequence encoding a signal polypeptide---, or ---a nucleic acid encoding purification epitope tag---, for example?

(b) Claim 1 (Claims 2-6 dependent therefrom) recites "the extracellular domain".

There is insufficient antecedent basis for this limitation in the claim. The term "the" refers to a specific extracellular domain and it is wholly unclear which specific extracellular domain is encompassed by the recited limitation.

(c) Claim 3 recites the limitation "the 32 terminal amino acids of the GPI-anchoring sequence". There is insufficient antecedent basis for this limitation in the claim.

It is unclear if the claims are limited to the one species disclosed in the specification such as SEQ ID NO: 3 (see instant Example 1) or to any other 32 terminal amino acids of a certain GPI-anchoring sequence.

Appropriate clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in

such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claim 5 recites "wherein said signal sequence is epidermal growth factor" wherein instant claims 1-4 and 6 are broad or broader to encompass the limitation of claim 5.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (*Enzo Biochem* 63 USPQ2d 1609 (CAFC 2002)).

The instant specification teaches a method of preparing extracellular domain tethered to the outside of mammalian cell by GFI anchor by expressing a recombinant

fusion nucleic acid molecule encoding a fusion polypeptide comprising known signal sequence(s), known purification epitope tag, known sequence of extracellular domain of membrane protein and known GFI and/or sequence in many known mammalian host cell. However, the breath of claims includes the use of gene encoding any epidermal growth factor. To fully describe a genus of mutant recombinant nucleic acid molecules, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. However, the instant specification or the prior art also do not describe single species of epidermal growth factor having a function of directing a fused partner polypeptide to endoplasmic reticulum so that it will be presented in the outside of mammalian host cell. *University of Rochester v. G.D. Searle & Co.* (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from *Enzo Biochemical* (see above).

Applicants and prior art do not describe any structure of epidermal growth factor in correlation with a function as signaling peptide; in turn there is no correlation between structure and function of the nucleic acid sequence encoding said any epidermal growth factor. Because the claims encompasses a method of using epidermal growth factor structure which do not function as signaling peptide, the one skilled in the art would not be in possession of full scope of the claimed genus of the instant specification.

9. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for a method for generating tethered extracellular domains of transmembrane protein by preparing an expression vector having a known signal sequence at 5'; does not reasonably provide enablement for method of preparing an expression vector having any epidermal growth factor sequence encoding nucleic acid as a signal sequence at 5' for generating tethered extracellular domains of transmembrane protein.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Instant claim 5 recites "wherein said signal sequence is epidermal growth factor" wherein instant claims 1-4 and 6 are broad or broader to encompass the limitation of claim 5.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of the invention is drawn to a method of preparing extracellular domain tethered to the outside of mammalian cell by GFI anchor by expressing a recombinant fusion nucleic acid molecule encoding a fusion polypeptide comprising known signal sequence(s), known purification epitope tag, known sequence of extracellular domain of membrane protein and known GFI and/or sequence in many known mammalian host cell. However, the breath of claims includes using any epidermal growth factor encoding nucleic acid to be used as signal sequence. The instant specification or the prior art do not describe any nucleic acid encoding epidermal

growth factor (EGF) wherein said EGF is used as signaling peptide for exporting out from the host mammalian cell, for example. Applicants and prior art disclose no direction or guidance as to how make and use a EGF as signaling peptide for directing localization of a fusion polypeptide thereof and/or exporting out a fusion polypeptide thereof from the host mammalian cell, for example. The instant specification do not disclose a single working example of nucleic acid molecule encoding EGF as signaling sequence. Thus, it is unpredictable to make and use the claimed nucleic acid encoding any EGF as a signal sequence in claimed method. The said unpredictability makes the relative skill required in the art very high. For all of the above reason, it would require undue experimentation necessary for claimed recombinant nucleic acid.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Kingsman et al. (WO03/089649; Published Oct. 30, 2003; as cited in the IDS).

Kingsman et al. teach an expression vector, methods of use and products obtained therefrom (see top of page 1); wherein the method of use which comprises (a) providing an expression vector (b) transfecting a host cell with the expression vector

(see claim 11 and 12 on page 68, for example); wherein the host cell includes CHO mammalian cells (see page 22, line 12). The expression vector by Kingsman et al. includes "an expression vector comprising an amino-terminal tag sequence and a signal sequence operably linked to a nucleotide sequence of interest" (see page 4, lines 12-14); wherein the gene of interest includes the h5T4 human protein with or without the transmembrane domain (see Figure 2 and its description of Figure 2 on page 7). The term "anchor" has been defined as "a sequence for attaching or associating a membrane protein domain with a lipid or lipid bilayer" (see page 4, lines 12-13); thus, includes, but not limited to, any transmembrane domain which associates with lipid bilayer of cell. The "extracellular domain" and transmembrane domain (TM) as shown Figure 2 of Kingsman et al. meet the instant "extracellular domain" and instant "anchor sequence" in instant claim 1, respectively.

11. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Fayen et al. (Methods in Enzymology, 2000, Vol. 327, pages 351-368).

Fayen et al. teach a recombinant fusion protein production by method involving a preparation of "Chimeric cDNAs encoding GPI-modified polypeptides can be prepared by several approaches" (see page 355, lines 8-9) such as engineering by polymerase chain reaction (PCR)-based splice by overlap extension as shown in a vector of Fig 2 (see page 355, lines 13-14). Fayen et al. teach the use of "an expression vector upstream of the GPI-signaling sequence of DAF on page 362, lines 6-7, for example, which was expressed on the surface of transfected cells. Fayen et al. teach CHO

mammalian cell line one of most widely employed cell lines for GPI anchored protein production (see bottom, page 358). Fayen et al. teach "It is critical that the polypeptide fusion partner selected for GPI anchoring have an N-terminal signal peptide that initially directs it into the lumen of the ER" that is 5' signal in a corresponding DNA (see page 355, lines 17-19) and teach an example of hybrid DNA in Fig. 3 having CD8 α (the extracellular domain), his6 and DAF GPI modifying sequence expressing GPI-modified CD8 α -His6 fusion protein at the surface of transfected cells (see Fig3 and its description on page 367). Fayen et al. also teach "Because the polypeptide of interest must have an N-terminal signal sequence, a substitute signal sequence (e.g., that of oncostatin M) can be appended to the N-terminal sequence of the polypeptide", and CD8 α has intercellular adhesion domain of v-homology domain (see middle and bottom of page 361). Thus, the method disclosed in Fayen et al. meets all limitations of claims 1, 2, 4 and 6. Because, the 32 terminal amino acid of the GPI-anchoring sequence is unclear as noted in rejection above under 35 U.S.C. 112, second paragraph; and no amino acid sequence structure is required in claim 3; claim 3 is included in instant rejection.

Additional References

Kennard et al. Animal Cell Biotechnology: Methods and Protocols, Humana press, (1999-B), pages 201-209.

Kennard et al. Animal Cell Biotechnology: Methods and Protocols, Humana press, (1999-A), pages 187-200.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 10AM-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656